UniProtKB/Swiss-Prot entry P05067

Entry information

Entry name	A4_HUMAN
Primary accession number	P05067
Secondary accession numbers	P09000 P78438 Q13764 Q13778 Q13793 Q16011 Q16 Q16019 Q16020 Q9BT38 Q9UCA9 Q9UCB6 Q9UCC8 Q9UCD1 Q9UQ58
Integrated into Swiss-Prot on	August 13, 1987
Sequence was last modified on	November 1, 1991 (Sequence version 3)
Annotations were last modified on	February 26, 2008 (Entry version 148)

Name and origin of the protein

Protein name	Amyloid beta A4 protein [Precursor]
Synonyms	APP ABPP Alzheimer disease amyloid protein Cerebral vascular amyloid peptide CVAP Protease nexin-II PN-II APPI PreA4
	Soluble APP-alpha (S-APP-alpha) Soluble APP-beta (S-APP-beta)

Q13625:TP53BP2; NbExp=2; IntAct=EBI-77613, EBI-77642;

- *SUBCELLULAR LOCATION*: Membrane; Single-pass type I membrane protein. Note= surface protein that rapidly becomes internalized via clathrin-coated pits. During matura the immature APP (N-glycosylated in the endoplasmic reticulum) moves to the Golgi complex where complete maturation occurs (O-glycosylated and sulfated). After alpha-secretase cleavage, soluble APP is released into the extracellular space and the C-tern is internalized to endosomes and lysosomes. Some APP accumulates in secretory tran vesicles leaving the late Golgi compartment and returns to the cell surface. Gamma-CT peptide is located to both the cytoplasm and nuclei of neurons. It can be translocated tc nucleus through association with Fe65. Beta-APP42 associates with FRPL1 at the cell surface and the complex is then rapidly internalized. APP sorts to the basolateral surfac epithelial cells. During neuronal differentiation, the Thr-743 phosphorylated form is loca mainly in growth cones, moderately in neurites and sparingly in the cell body. Casein ki phosphorylation can occur either at the cell surface or within a post-Golgi compartment.
- *ALTERNATIVE PRODUCTS*: 10 named isoforms [FASTA] produced by alternative spli Additional isoforms seem to exist. Experimental confirmation may be lacking for some isoforms.

Name APP770
Synonyms PreA4 770
Isoform ID P05067-1
Note: A major isoform. ⇐
This is the isoform sequence displayed in this entry.

Name APP305
Isoform ID P05067-2
Features which should be applied to build the isoform sequence: VSP_000005, VSP_000006.

Name L-APP677
Isoform ID P05067-3
Note: The L-isoforms are referred to as appicans.
Features which should be applied to build the isoform sequence: VSP_000002, VSP_000004, VSP_000009.

Name APP695
Synonyms PreA4 695
Isoform ID P05067-4
Note: A major isoform. ⇐
Features which should be applied to build the isoform sequence: VSP_000002, VSP_000004.

Name L-APP696
Isoform ID P05067-5
Note: The L-isoforms are referred to as appicans.

Features which should be applied to build the isoform sequence: VSP_000002, VSP_000003, VSP_000009.

Name APP714
Isoform ID P05067-6
Features which should be applied to build the isoform sequence: VSP_000002, VSP_000003.

Name L-APP733
Isoform ID P05067-7
Note: The L-isoforms are referred to as appicans.
Features which should be applied to build the isoform sequence: VSP_000007, VSP_000008, VSP_000009.

Name APP751
Synonyms PreA4 751
Isoform ID P05067-8
Note: A major isoform. ⟸
Features which should be applied to build the isoform sequence: VSP_000007, VSP_000008.

Name L-APP752
Isoform ID P05067-9
Features which should be applied to build the isoform sequence: VSP_000009.

Name APP639
Isoform ID P05067-10
Features which should be applied to build the isoform sequence: VSP_009116, VSP_009117, VSP_009118.

- *TISSUE SPECIFICITY*: Expressed in all fetal tissues examined with highest levels in br kidney, heart and spleen. Weak expression in liver. In adult brain, highest expression fc in the frontal lobe of the cortex and in the anterior perisylvian cortex-opercular gyri. Moc expression in the cerebellar cortex, the posterior perisylvian cortex-opercular gyri and tl temporal associated cortex. Weak expression found in the striate, extra-striate and mot cortices. Isoform APP695 is the predominant form in neuronal tissue, isoform APP751 a isoform APP770 are widely expressed in non-neuronal cells. Isoform APP751 is the mo abundant form in T-lymphocytes. Appican is expressed in astrocytes.
- *INDUCTION*: Increased levels during neuronal differentiation.
- *DOMAIN*: The basolateral sorting signal (BaSS) is required for sorting of membrane prc to the basolateral surface of epithelial cells.
- *DOMAIN*: The NPXY sequence motif found in many tyrosine-phosphorylated proteins is required for the specific binding of the PID domain. However, additional amino acids eit N- or C-terminal to the NPXY motif are often required for complete interaction. The PID domain-containing proteins which bind APP require the YENPTY motif for full interactio These interactions are independent of phosphorylation on the terminal tyrosine residue.